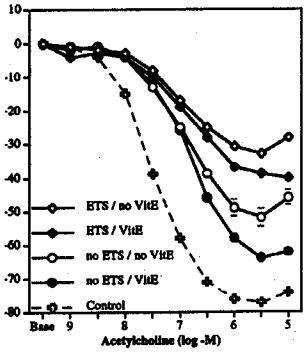
were contracted with phenylephrine (Phe), and Phe-precontracted rings were relaxed with acetylcholine (ACh) and the calcium-ionophore A23187. Aortic superoxide anion (SO) formation was measured using a lucigenin chemiluminesence technique. Results were analyzed with a general linear model ANOVA. ETS and HC increased SO ($p = 0.005$ and $p = 0.03$) and impaired ACh ($p = 0.002$, $p = 0.02$) and A23187-induced relaxation ($p < 0.005$, $p = 0.003$). Vit E blocked the effect of ETS on ACh-induced ($p = 0.048$), but not on A23187-induced relaxation, nor on SO formation. ETS is an oxidant stress on endothelium, and impairs endothelium-dependent relaxation. Vitamin E/beta-carotene at this dose confers only modest protection against ETS-induced endothelial dysfunction.



1007-173 Insulin Induced Vasodilatation of Internal Carotid Artery

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Insulin increases leg and forearm blood flow in humans, this may be secondary to its effect on glucose uptake by muscle. To demonstrate that this effect of insulin is independent of its metabolic action, we assessed the internal carotid artery diameter during systemic insulin infusion as glucose uptake in the brain is not dependent on insulin. Eight healthy males were infused, 3 units of regular insulin with 125 ml of 10% Dextrose and 5 mmol of potassium chloride, over one hour. A 7.5 mHz linear array transducer linked to 128XP Acuson ultrasonograph was used to monitor the internal carotid artery diameter. The internal carotid artery diameter increased from a mean of 5.9 ± 0.9 mm to 6.9 ± 0.8 mm, an increase of $17 \pm 5\%$ ($p < 0.05$) and regressed back to the baseline within 15 minutes of stopping the infusion. Plasma glucose was maintained between 93 to 105 mg/dl. Insulin levels increased from 14 to 47 μu/ml within 30 minutes and stabilized thereafter.

Time	0 min	15 min	30 min	45 min	60 min	75 min
Diameter (%)	100 (5.9 mm)	104	110*	113*	117*	99

[The diameter is expressed as percentage of basal. The change in diameter (one-way ANOVA) is statistically significant, $p < 0.05$*.] We conclude that insulin dilates internal carotid artery within 30 minutes and this continues throughout the period of insulin infusion. This effect occurs at physiological insulin levels and is independent of its metabolic action. Resistance to this effect of insulin may be of relevance in the pathogenesis of cerebral blood flow abnormalities in the NIDDM.

1007-174 Impaired Endothelial Relaxation Associated with Insulin Resistance Is Not Due to Nitric Oxide

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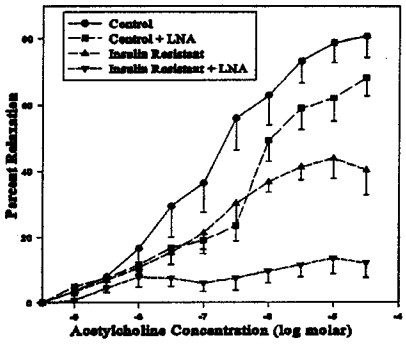
The insulin resistant syndrome is causally related to hypertension and cardiovascular events, however, the underlying mechanism(s) remain unknown. We have previously demonstrated impaired endothelial relaxation in a rat model of insulin resistance (IR). This study evaluates if a nitric oxide (NO) deficit is caused by IR. Sprague Dawley rats were randomized into two groups: (1) control (C) ($n = 16$) or (2) IR ($n = 15$). Insulin resistance was induced by fructose rich diet. Intraluminal diameter was measured (in vitro) in mesenteric arteries (200–250 μM) maintained at a constant intraluminal pressure of 40 mmHg. Impaired endothelial function was present in 80% of IR rats; these data are presented. Vessels were constricted with phenylephrine and endothelial mediated relaxation to acetylcholine (Ach) was determined ± pretreatment with n-Nitro-L-arginine (LNA), a NO synthase inhibitor. The dose response curves are in the graph. Maximal relaxation (Emax) in C vessels was not affected by LNA (mean ± SEM) (80 ± 7 vs $68 \pm 7\%$). However, Emax in IR vessels was impaired by LNA (40 ± 8 vs $12 \pm 5\%$ ($p < 0.05$)).



These data suggest that relaxation to Ach in IR vessels is dependent on NO, whereas relaxation in C vessels is not. Thus, the impairment in endothelial dependent relaxation in insulin resistance is due to endothelial derived relaxant factors other than NO, such as endothelial derived hyperpolarizing factor or prostacyclin.

1007-175 Reduced Vasodilator Responses to Nitroprusside or Nitroglycerin After Diaspirin Crosslinked Hemoglobin (DCLHb™) in Open-Chested Swine

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Several commercial hemoglobin products increase mean systemic arterial pressure (MAP) and systemic vascular resistance (SVR), most likely due to hemoglobin-mediated inactivation of nitric oxide (NO) released by endothelium. NO inactivation by extraerythrocytic hemoglobin might also interfere with the vasorelaxant effects of nitrovasodilators, antihypertensive agents whose efficacy involves NO release. To evaluate this possibility, we measured vasodilator responses to sodium nitroprusside (SNP), 3 and 10 μg/kg/min i.v., and nitroglycerin (NTG), 10 and 30 μg/kg/min i.v., before and after DCLHb, 0.3 g/kg i.v., in 12 anesthetized, open-chested swine. DCLHb raised MAP by 21 ± 2 mm Hg (SE) and SVR by 1442 ± 105 dyne cm sec^{-5} from pretreatment baseline values of 84 ± 3 and 3059 ± 288. The following mean changes (Δ) ± SE occurred with SNP or NTG:

	ΔMAP (mm Hg)	ΔSVR (dsc^{-5})
Before DCLHb		
SNP 10 μg/kg/min	-36 ± 2	-1447 ± 159
NTG 30	-27 ± 3	-1257 ± 171
After DCLHb		
SNP 10	-11 ± 2*	-701 ± 140*
NTG 30	-12 ± 2*	-671 ± 94*

*$p < 0.03$ vs. value before DCLHb

DCLHb similarly reduced vasodilator responses to lower as well as higher doses of either SNP or NTG. However, vasodilator responses were unchanged when SNP and NTG were repeated after human serum albumin, 0.25 g/kg i.v., in 5 control swine. Our data show that the vasorelaxant effects of SNP and NTG are markedly diminished after a moderate dose of DCLHb, suggesting that these nitrovasodilators have limited antihypertensive efficacy in the presence of DCLHb. This may, in part, reflect DCLHb-mediated inactivation of NO release induced by nitrovasodilators.

1007-176 Physiologic Concentrations of Estradiol Attenuate Endothelin-induced Coronary Vasoconstriction In Vivo

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Estrogens are cardioprotective and are reported to have anti-anginal properties. We examined the effect of physiologic doses of 17β-estradiol (E) on coronary response in 12 anesthetized female pigs. Epicardial cross-sectional area (CSA) was assessed by intracoronary ultrasound, average peak flow velocity (APV) by Doppler guidewire, and coronary blood flow (CBF) was calculated. Intracoronary dose response curves to ET-1 (1 pm to 10 nM), sarafotoxin (SFT) (1 pm to 10 nM) and serotonin (5HT) (0.1 nM to 1 μM) were assessed before and after a 10 minute infusion of E (1 nM). Prior to E administration, ET-1 induced significant dose-dependent decreases in CSA, APV, and CBF, all of which were attenuated following E (see table).